**NANOTECHNOLOGY IN DISEASE DIAGNOSIS**

*Lakshika Bhandaria , Kanchan Karki\* b , Aman Sharmac , Shivanand Tripathid*

a Young Professional I, Molecular Biology and Genetic Engineering Laboratory, Uttarakhand Council for Biotechnology, Biotech Bhawan, Haldi, Uttarakhand, India

b Scientist B, Molecular Biology and Genetic Engineering Laboratory, Uttarakhand Council for Biotechnology, Biotech Bhawan, Haldi, Uttarakhand, India

c Research Trainee, Uttarakhand Council for Biotechnology, Biotech Bhawan, Haldi, Uttarakhand, India

d APJ Abdul Kalam Technical University, Lucknow

\* Corresponding author: Scientist B, Molecular Biology and Genetic Engineering Laboratory, Uttarakhand Council for Biotechnology, Biotech Bhawan, Haldi, Uttarakhand, U.S. Nagar, 263145, India; Tel.: +9412966148; Fax: +05944-230567, E-mail: ksinghbiophysics@gmail.**com**

**INTRODUCTION**

NNI or National Nanotechnology Initiative defined nanotechnology as the study of every element that is about 100 nanometers or less. A nanometer is 1 billionth of a meter in size [1]. In minor element dimension, the proportion of exterior atoms/molecules to the entire quantity amplify is one of the biggest advantages which results in having a great surface area which direct it to enlarge the surface movement also generating modifications in the biological characteristics as well as physical characteristics. Some other advantages of nanoparticles are:

* Sustained and inhibited release
* Super bioavailability
* Capacity to target
* Abridged toxicity
* Inexpensive
* Improved the permeability
* More accurate and less invasive surgery
* Provide effective freedom to the brain and intracellular compartment
* Faster dissolution especially in the internal aqueous fluid
* Faster, safer and more accurate disease diagnosis
* Large scale production is feasible
* Stability of drugs in biological fluids so that it can prevent pain at the injection site
* Allergic reactions [2]

Solid-state nanopores within graphene-based materials are on the brink of basically changing the sensing of required bioanalytes through ion trafficking across nanoporous membranes [3]. Nanotechnology that deals with the nano particles is not only limited to research field but also in various day-to-day activities. Nanotechnology together as diagnosis as well as treatment of disease is acknowledged as nanomedicine. Nano-technology is enormously essential for detecting communicable diseases in addition to viruses [4].

1. **Nanoparticles: Role in Disease Diagnosis and Treatment**

Earlier nanotechnology is used in various other fields but the use of this technology in medicine is latest. The major purpose of medicine is early finding of health issues and providing suitable treatment. If nanotechnology is connected with medicine, the treatment of disease is more effective [5]. Cancer, diabetes, depression and many other diseases are very common with fast moving life. Nanotechnology in the form of nanorobots, microchips and biosensor are mostly used for diagnostic purpose [6]. Various issues are related with the old methods, it may destroy the healthy tissues owing to toxicity sourced by the drug. However nanoparticles using eco-friendly polymers are further efficient moreover eliminate the trouble [7]. Quantum dots which are nanoparticles fabricated, when placed in UV light absorb light and glow. When these nanoparticles are moved towards the inner cancerous cell then these quantum dots starts glowing and tells about the tumor. For in vivo and vitro study various nanoparticles are used [8]. Many nanoparticles are used in infectious and inflammatory diseases.

**Hepatitis** is the infectious disease which is caused by the virus. It is chronic disease which is associated for whole life. Nanoparticles can be used for the diagnosis of this disease. Gold nanoparticles are more preferable for this purpose. Gold nano-protein chips are formed, which detect the antibodies for hepatitis. So, these chips are effective in diagnostic purpose. For treatment purpose, DNA vaccine coated SiO2 (LDH) nanoparticles induced antibody is used mostly [9].

Nanotechnology is also used in treatment of **bone inflammation**. Metal nanotechnology is most effective in osteoblasts formation. These nanoparticles provide more surface area for osteoblasts formation in proper manner. Titanium (Ti) is usually used nonmaterial for the bone inflammation. Super paramagnetic iron oxide nanoparticles are linked with the PLGA particles used in joint inflammation [10].

Nanotechnology is also effective in **skin infection**. One of the medicines used for the treatment of skin infection is nitric acid coated nanoparticles. Iron oxide nanoparticles have direct link with protein thrombin which provides protection against anti thrombin because it takes part in process of tissue repair. Nanoparticles help together as anti-inflammatory drugs in penetrating the skin [11]. Noble metals and their composite are used as healing agents in earlier time as a medicine for many diseases.

In the **dental field**, nanotechnology help in production of nano-filled resin compound that contain small size packing particles which liquefy in higher concentration and deposited the hydroxyapatite on enamel. Pt Nps are used for enamelling process that enhances the strength of teeth [12].

Nanotechnology also plays important role in **cardiovascular and pulmonary diseases**. Nanomaterials are used to improve the heart muscles function. For this purpose, carbon nanofibers enclosed with PLGA enhances the heart muscles growth. Carbon nanotubes are the more advanced form due to their unique electrical, thermal and mechanical properties. Carbon nanotubes are specially functionalized for transport of drugs. Nano-pillars and nano-lines are effectively used in fibroblast that is most effective to check the proliferation of lung carcinoma cell lines. For this purpose choice of nano roughness and nano spherical surfaces is most significant [13].

Drug delivery is one of the most important aspect, especially in the research field and has more application in clinical field. For this purpose many nanoparticles are used for delivery of drugs in the diseased part of the body. For this many nanoparticles are used but more preferable nanoparticles are gold nanoparticles (Au NPs). We can use gold nanoparticles in drug delivery because of many advantages

* can easily synthesized in the nano range such as rod like and cage like
* due to the presence of negative charge on surface of nanoparticles they can easily functionalized with any biomolecules
* Less toxic and so on. For proper delivery of drugs, nanoparticles is functionalized with biomolecules such as DNA enhancing the modification.

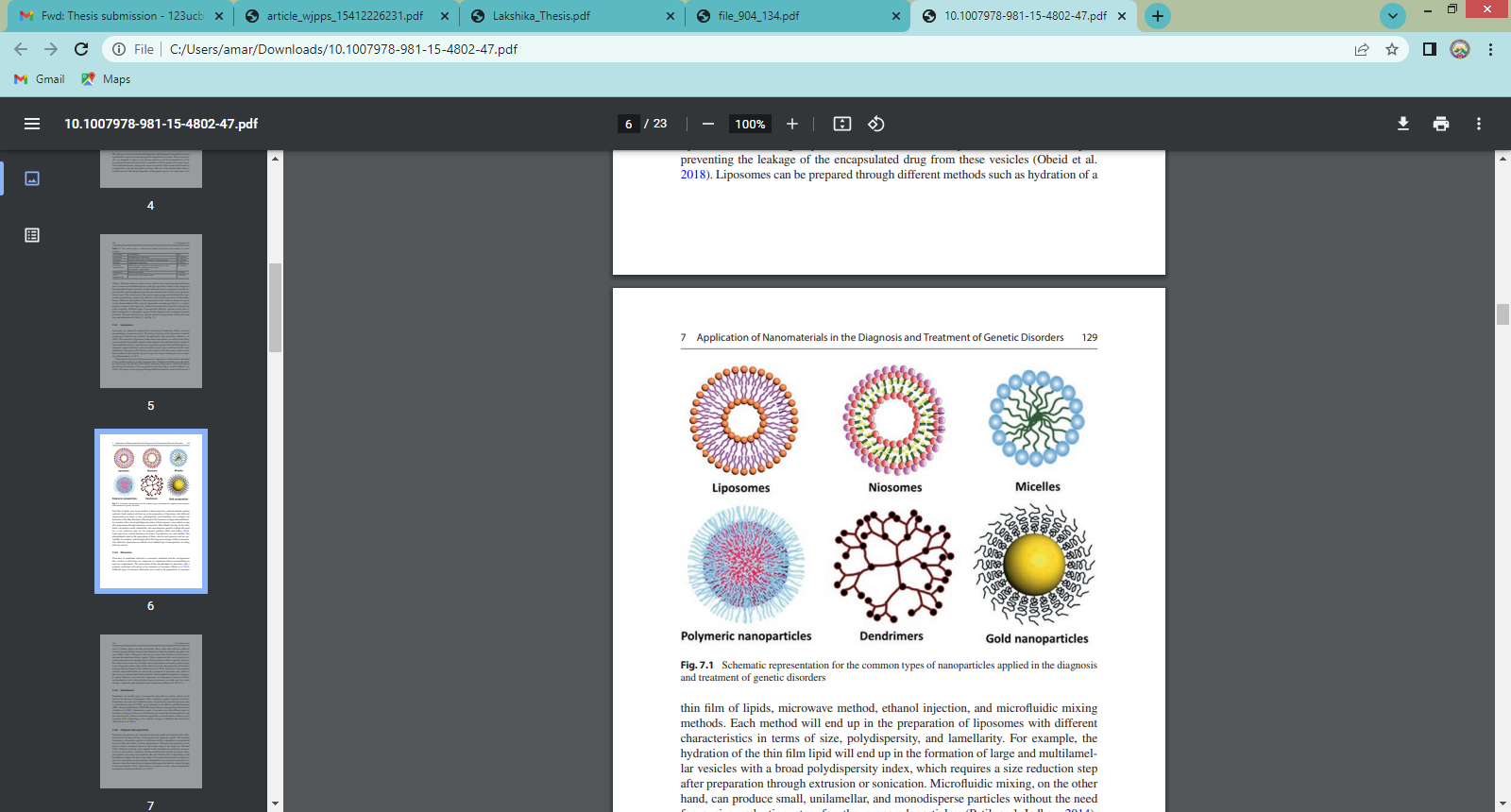
Gene therapy is an approach for the treatment of genetic diseases. For this, oligonucleotides like DNA, RNA and plasmids have healing effects. Gold nanoparticles are an ideal for RNA and DNA delivery. Oligonucleotides act as intra cellular regulatory agents. Gold nanoparticles surface is modified with the attachment of oligonucleotides. These enhance the property of NPs. These modified gold nanoparticles are important in development of therapy and gene delivery [14].

Nanoparticles are used in **Alzheimer’s disease (AD)** cure. Alzheimer’s disease (AD) is known as one of the most frequent diseases in early age people and is a serious problem in 35 million people about all over the world. The effects of this disease are increasing every year. For this purpose, many nanoparticles are used including, zinc and silver oxide, titanium oxide and silica dioxide. Many works have been done on bioactive compounds like flavonoids and selenium with oxidant nanoparticles used in treatment of Alzheimer’s disease. Nanoparticles affects on brain by increase the amount of production of reactive oxygen species by decrease in production of amyloid β (Aβ). This disease is caused due to accumulation of amyloid β (Aβ) in the brain. So, selenium rich nanoparticles are more effective in cure of (AD) [15].

**Kidney disease** is one of the serious diseases. It is common chronic disease. Magnetic resonance imaging (MRI) is the technique used for the treatment and investigation. This technique provides information about function and structure of kidney. MRI is using nanoparticles in addition to it [16]. **Oral cancer** is the sixth common disease present in the world. There are 5% chances to cure about this disease and requires early detection. There are many techniques which are used in the detection of disease. Most commonly used techniques are MRI, Raman spectroscopy and PET. But these methods not gave early detection about disease. When antibody bonding gold nano rods is employed in Raman spectroscopy, it will give sharper and better result

1. **Different Nanoparticles Used in Diagnosis as well as Cure of Genetic Disorders**

To improve the effectiveness of therapeutic preparations and many conventional diagnostics nanoparticle drug delivery system can be used. Nanoparticles are designed in such a way that they can be used to improve the pharmacokinetics, the bio-distribution of the encapsulated agents. Usually, these diagnostic agents are either encapsulated inside or attached to a specific drug delivery carrier. Therapeutic agents and diagnostics can be delivered by the nanoparticles delivery systems which can range from 10-300 nm. Through this size (at nano level), these carriers will be able to go through unhealthy tissues such as inflamed tissues or tumors and with elevated specificity on the basis of changes in the pathophysiological structure in these diseased tissues in contrast to healthy tissues that hive usual tight junctions that put off molecules at this size to go through these tissues. This is the basis of the passive targeting approach that helps the nano-carriers drug delivery system to be selective to diseased tissue as well as evade the healthy tissues. Furthermore, the surface of the nano-carriers used to transport diagnostic agents can be functionalized with a precise ligand which binds specifically to a complementary receptor at the target site, which will enhance their specificity through the active targeting. Therapeutic agents and diagnostics can be delivered by the various types of nanoparticle delivery systems used for the diagnosis and treatment of genetic disorders.



**Fig1 Schematic depiction for the common types of nanoparticles applied in the diagnosis moreover cure of disorders**

**II.a. Liposomes**

Liposomes are spherical nanoparticles composed of membrane bilayer structures that encapsulate aqueous entities. The bilayer structure of the liposomes is usually composed of natural and synthetic phospholipids, includes cholesterol [17]. This liposomal structure makes these nanocarriers multipurpose as they can encapsulate hydrophilic drugs in the aqueous core plus hydrophobic drug in the membrane bilayer. Liposomes are expected to guard the loaded therapeutic or else diagnostic agent until these carriers attain the target tissue in addition to adhere to the outer membrane of the target cell. Additionally, the surface of the liposomal vesicles can be functionalized with precise ligands for specific receptor binding for active targeting [18]. Liposomes have some restrictions related to making costs and stability. The phospholipids used to manufacture these vesicles are pricey as well as prone to oxidation, which can influence the long-term storage of these nanoparticles. Nonetheless, liposome is still the largely studied type of nanoparticles as drug delivery systems.

**II.b. Niosomes**

Liposome-like vesicles, also called niosomes**,** or nonionic detergent vesicles, consist of a membrane bilayer that encapsulates an aqueous compartment. Niosomes are formed when the liposome phospholipids are replaced by nonionic detergents [19]. Other components that can be used in niosome preparation are charged lipids that are used to provoke specific charges on the surface of niosomes. For instance, diacetyl phosphate has been used to create negatively charged niosomes, and sterilized amines have been used to create surface positively charged niosomes [20]. Niosomes are superior to liposomes in terms of stability and manufacturing cost because the surfactants used in niosomes are steady as well as greatly cheaper in contrast to the phospholipids used in liposomes[21].

**II.c. Dendrimers**

Dendrimers are a specific class of nanoparticle drug delivery systems that can also be used todeliver therapeutics and/or diagnostics for genetic diseases**.** These are various types of repeatedly branched polymers using different step-growth polymerizations**,** such as PEG (poly (ethylene glycol), PEI (polyethyleneimine), PGA (poly (l-glutamic acid), as well as PAMAM (polyamidoamine). [22]. A dendrimer consists of an inner core with various levels of branching emerging from this core. Dendrimers are monodisperse nanoparticles, and the outer ends of these branched nanoparticles can be tailored to accomplish active targeting of charged drugs or selective imaging of various unhealthy tissues [23].

**II.d. Polymeric Nanoparticles**

One of the most thoroughly studied solid colloidal particles for the delivery of therapeutic as well as diagnostic substances is polymeric nanoparticles. These nanoparticles surfaces will be conjugated or encapsulated with the targeted medicinal or diagnostic substances to be given. To attain sustained discharge of the loaded payload at the target region, polymeric nanoparticles can be utilised [24]. Emulsification, solvent extraction, nanoprecipitation, along with other techniques can be used in the creation of polymeric nanoparticles for drug delivery [25]. The ultimate composition of the manufactured polymeric nanoparticles may be nanocapsules or nanospheres, depending on the formulation procedure. Polymeric nanoparticles will shield the diagnostic or therapeutic chemicals from the body's enzymes' tendency to degrade them. Diffusion, hydrolysis, enzymatic degradation, or a combination of all these processes will be used to release the loaded payload from the polymeric nanoparticles [26]. PLA (polylactide), PLGA (Poly (lactide-co-glycolide), PCL (polyglycolide, polycaprolactone), poly (d,l-lactide), in addition to many other types of polymers can be utilised to create polymeric nanoparticles. For the creation of polymeric nanoparticles with active targeting, polyethylene glycol can also be added [27].

**II.e. Micelles**

Micelles are a drug delivery system in which amphiphilic molecules will be self assembled into spherical particles. The type of these amphiphilic molecules in micelles preparation will decide the final micelles category which includes lipid-polymeric hybrid micelles, lipid micelles, or polymeric micelles. The hydrophobic portion of the copolymer will make up the core of these monolayer vesicles, whilst the hydrophilic portion will be uncovered to the surrounding aqueous environment [17]. The most minuscule concentration of these molecules necessary for micelle vesicle production and self-assembly is known as the critical micelle concentration (CMC), and it is what determines whether a micellar structure will form [28]. Hydrophobic therapeutic or diagnostic substances can be confined inside the micelle's core and shielded from the degradative enzymes on the outside in the micellar structure [29]. However, micelles often have a limited capability for loading hydrophobic therapeutic or else diagnostic substances due to their low hydrophobic volume [17].

**II.f. Gold Nanoparticles (AuNPs)**

AuNPs are regarded as eye-catching drug delivery systems for delivering a variety of molecules like proteins, nucleic acids plus anti-cancer drugs**.** The cores of these NPs are non-toxic as well as inert. Furthermore, these NPs can be effortlessly produced in various sizes ranging from 1 to 200 nm with a mono disperse size distribution [30]. AuNPs can be prepared by reducing gold salts byadding reducing agent in the presence of stabilizers to prevent aggregation**.** The final unit size of these NPs depends on the nature of the gold salt and stabilizer used**.** By conjugating drugs to these nanoparticles via thiol linkages**,** these NPs can distribute various therapeutic and/or diagnostic agents. Gold nanoparticles have been examined by many investigatorsasdelivery vehicles for X-ray contrast agents [31], immunostaining [32], and many therapeutic agents to facilitate uptake by target cells [33, 34].

**Conclusions**

Nanoparticles due to their small size have more surfaces to volume ratio. The surface provides larger area for chemical reaction. Nanoparticles made drug delivery easy in a specific way. They have been used in many methods as well as in many types of equipments which made them very effective. Though they are not very cheap but they increase the sensitivity. Due to SPR and fabrication properties of silver nanoparticles, these are used in bioengineering, optoelectronic, medicine nanotechnology and other advanced fields. Recently, silver nanoparticles have been used as antifungal and antibacterial agent. Through this, early findings of the diseases (like cancer) are very important. They are very effective in kidney and gastrointestinal diseases. The proteins and other molecules which get attached with nanomaterials and permit it to find the initial stages of the disease. There are many systems that have been developed to detect disease under the nanomaterial. About them, one is nano sphere, that uses AuNPs. Carbon nanotubes as well as gold nanoparticles are widely used as biosensor that detects proteins responsible for oral diseases. Viruses and other microscopic components from blood samples are separated by using Ag nanorods. This can be monitored by Raman spectroscopic signals. Recent developments in nanotechnology over the past two decades have encouraged the researchers in the field to develop new and extremely trustworthy methods for illness diagnostics. It is not surprising that the field of illness diagnostics has frequently changed due to the quick breakthroughs and inventions in nanomedicine. The application of nanotechnology in the field of nanomedicine is well established in biomedical research and clinical practise, and in the coming years, it may have a significant impact on human health. Imaging and the targeted application of nanoparticles from medication carriers are frequently employed in diagnosis. Through nanoscale sensors and tools continuous clinical care are provided for patients health. In the early stages of diseases such as leukemia and inflammation, nanoscale detectors and software are helping to improve diagnosis. However, nanomaterials have provided significantadvances in disease diagnosis and have become important interventions in modern medicine.

**References**

1. NagaVerma B., Hement K. and Ayaz A. 2012. Different techniques for preparation of polymeric nanoparticles- A review. Asian Journal of Pharmaceutical and Clinical Research. 5:17-23. 9.
2. Abhilash M. 2010. Potential applications of naroparticles. The International Journal of Pharma and Bio Sciences. 1(1):1-12. 10.
3. Anuj Nehra, Weizao Chen, Dimiter S. Dimitrov, Anu Puri, Krishna Pal Singh. 2017. Graphene Oxide-Polycarbonate Track-Etched Nanosieve Platform for Sensitive Detection of Human Immunodeficiency Virus Envelope Glycoprotein. ACS Applied Materials & Interfaces. 9(38):32621–32634.
4. Lakshika Bhandari, Shalini Singh, Lalit Dumka, Kanchan Karki. 2022. COVID-19 and Nanobiosensors. Role of Biotechnology in Covid Vaccine Development. ABS Books. ISBN 978-93-91002-91-6.
5. Sanvicens, N. and M.P. Marco. 2008. Multifunctional nanoparticles–properties and prospects for their use in human medicine. Trends in biotechnology. 26(8): 425-433.
6. Cuenca, A.G. 2006. Emerging implications of nanotechnology on cancer diagnostics and therapeutics. Cancer. 107(3):459-466.
7. Ringsdorf, H. 1975. Structure and properties of pharmacologically active polymers. Journal of Polymer Science Polymer Symposia. 51(1):135 – 153.
8. Kircher, M.F. 2003. A multimodal nanoparticle for preoperative magnetic resonance imaging and intraoperative optical brain tumor delineation. Cancer research. 63(23):8122-8125.
9. Klippstein, R. and D. Pozo. 2010. Nanotechnology-based manipulation of dendritic cells for enhanced immunotherapy strategies. Nanomedicine: Nanotechnology, Biology and Medicine. 6(4):523- 529.
10. Baghaban-Eslaminejad, M. 2017. The role of nanomedicine, nanotechnology, and nanostructures on oral bone healing, modeling, and remodeling, in Nanostructures for Oral Medicine. Elsevier. 1:777-832.
11. Ikoba, U. 2015. Nanocarriers in therapy of infectious and inflammatory diseases. Nanoscale. 7(10):4291- 4305.
12. Rai, M. 2016. Strategic role of selected noble metal nanoparticles in medicine. Critical reviews in microbiology. 42(5):696-719.
13. Chun, Y.W.2013. Therapeutic application of nanotechnology in cardiovascular and pulmonary regeneration. Computational and structural biotechnology journal. 7(8):e201304005.
14. Kim, E.-Y. 2012 Gold nanoparticle-mediated gene delivery induces widespread changes in the expression of innate immunity genes. Gene therapy. 19(3): 347.
15. Nazıroğlu, M., S. Muhamad, and L. Pecze. 2017. Nanoparticles as potential clinical therapeutic agents in Alzheimer’s disease: focus on selenium nanoparticles. Expert review of clinical pharmacology. 10(7): 773-782.
16. Charlton, J.R., S.C. Beeman, and K.M. Bennett. 2013. MRI detectable nanoparticles: the potential role in the diagnosis of and therapy for chronic kidney disease. Advances in chronic kidney disease. 20(6):479-487.
17. Obeid MA, Tate RJ, Mullen AB, Ferro VA. 2018. Lipid-based nanoparticles for cancer treatment. In: Lipid nanocarriers for drug targeting. Elsevier. 1:313-359.
18. Akbarzadeh A, Rezaei-Sadabady R, Davaran S, Joo SW, Zarghami N, Hanifehpour Y, Samiei M, Kouhi M, Nejati-Koshki K. 2013. Liposome: classification, preparation, and applications. Nanoscale Research Letters. 8:102.
19. Obeid MA, Khadra I, Albaloushi A, Mullin M, Alyamani H, Ferro VA (2019) Microfluidic manufacturing of different niosomes nanoparticles for curcumin encapsulation: physical characteristics, encapsulation efficacy, and drug release. The Beilstein Journal of Nanotechnology. 10:1826–1832.
20. Marianecci C, Di Marzio L, Rinaldi F, Celia C, Paolino D, Alhaique F, Esposito S, Carafa M (2014) Niosomes from 80s to present: the state of the art. Advances in Colloid and Interface Science. 205:187–206.
21. Obeid MA, Khadra I, Mullen AB, Tate RJ, Ferro VA. 2017c. The effects of hydration media on the characteristics of non-ionic surfactant vesicles (NISV) prepared by microfluidics. The International Journal of Pharmaceutics 516:52–60.
22. Aulenta F, Drew MG, Foster A, Hayes W, Rannard S, Thornthwaite DW, Worrall DR, Youngs TG. 2005. Synthesis and characterization of fluorescent poly (aromatic amide) dendrimers. The Journal of Organic Chemistry. 70:63–78.
23. Kesharwani P, Jain K, Jain NK. 2014. Dendrimer as nanocarrier for drug delivery. Progress in Polymer Science. 39:268–307.
24. Masood F. 2016. Polymeric nanoparticles for targeted drug delivery system for cancer therapy. Materials Science and Engineering: C. 60:569–578.
25. Rao JP, Geckeler KE. 2011. Polymer nanoparticles: preparation techniques and size-control parameters. Progress in Polymer Science. 36:887–913.
26. Edlund U, Albertsson A-C. 2002. Degradable polymer microspheres for controlled drug delivery. In: Degradable aliphatic polyesters. Springer. 157:67-112.
27. Prabhu RH, Patravale VB, Joshi MD. 2015. Polymeric nanoparticles for targeted treatment in oncology: current insights. The International Journal of Nanomedicine. 10:1001.
28. Letchford K, Burt H. 2007. A review of the formation and classification of amphiphilic block copolymer nanoparticulate structures: micelles, nanospheres, nanocapsules and polymersomes. The European Journal of Pharmaceutics and Biopharmaceutics. 65:259–269.
29. Obeid MA, Elburi A, Young LC, Mullen AB, Tate RJ, Ferro VA. 2017a. Formulation of nonionic surfactant vesicles (NISV) prepared by microfluidics for therapeutic delivery of siRNA into cancer cells. Molecular Pharmaceutics. 14:2450–2458.
30. Ghosh P, Han G, De M, Kim CK, Rotello VM. 2008. Gold nanoparticles in delivery applications. Advanced drug delivery reviews. 60(11):1307–1315.
31. Hainfeld JF, Dilmanian FA, Slatkin DN, Smilowitz HM. 2008. Radiotherapy enhancement with gold nanoparticles. The Journal of Pharmacy and Pharmacology. 60(8):977–985.
32. Mallidi S, Kim S, Karpiouk A, Joshi PP, Sokolov K, Emelianov S. 2015. Visualization of molecular composition and functionality of cancer cells using nanoparticle-augmented ultrasoundguided photoacoustics. Photoacoustics 3(1):26–34
33. Jain S, Coulter JA, Hounsell AR, Butterworth KT, McMahon SJ, Hyland WB, Muir MF, Dickson GR, Prise KM, Currell FJ, O’Sullivan JM. 2011. Cell-specific radiosensitization by gold nanoparticles at megavoltage radiation energies. International Journal of Radiation Oncology - Biology - Physics 79(2):531–539.
34. Pissuwan D, Niidome T, Cortie MB. 2011. The forthcoming applications of gold nanoparticles in drug and gene delivery systems. The Journal of Controlled Release 149(1):65–71.